National Aeronautics and Space Administration
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John Glenn
Biomedical Engineering Consortium
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Biodosimeter for Ionizing Radiation in Space

A noninvasive biodosimeter that could be used as an alternative to current radiation exposure limits to determine exposure risk is being developed using the special properties of clusterin, a molecule that is secreted as a result of radiation exposure.

Exposure to cosmic radiation has been cited by NASA as a leading risk to astronauts, one that must be overcome before interplanetary travel can be undertaken. It is well known that exposure to radiation can increase the risk of cancer.

The standard dosimeters on the International Space Station measure the amount of radiation striking the inside of the spacecraft or an astronaut's body, from which the radiological burden and the individual's response must be deduced. This John Glenn Biomedical Engineering Consortium (GBEC) project's alternative approach is innovative in several ways.

Luciferase, which originates in fireflies, acts as a reporter gene. It expresses luciferase protein whenever the gene of interest is expressed. Luciferase protein and its substrate luciferin create light.

Principal investigator David L. Wilson, Department of Biomedical Engineering, Case Western Reserve University (CWRU) is collaborating with David A. Boothman (Radiation Oncology, University Hospitals of Cleveland and CWRU) and Andrew Rollins (Department of Biomedical Engineering, CWRU) to produce a noninvasive biodosimeter by using the special properties of clusterin, a molecule that is secreted as a result of radiation exposure. Secretory clusterin is produced by cells following exposure to very low levels of low linear energy transfer (LET) ionizing radiation. The luciferase reporter gene and bioluminescence molecular imaging will be used to determine clusterin production.

The luciferase gene, which enables imaging, originates in fireflies. It is introduced into the genome near a gene of interest, as a reporter gene. As a result, luciferase protein is expressed whenever the gene of interest is expressed. The protein and its substrate luciferin then produce light that can be imaged by a very sensitive camera. In our application, the interest is in clusterin. There are many other applications of this technology including cancer biology and assessment of gene delivery techniques.

If proven feasible, this biodosimeter should be more appropriate than a physical device for risk assessment and dose projection. It might predict radiation sickness and carcinogenesis for an individual. It also could be used as an alternative to current radiation exposure limits and help determine the limit beyond which a mission must be cancelled.

Experiments on Earth will determine clusterin production dose response for low and high LET radiation in a mouse model. Using protein fusion technology, researchers will later determine serum clusterin levels. These experiments will allow a better understanding of in vivo secretory clusterin production and biodistribution.

To carry out this work, an imaging system will be constructed consisting of a cooled charge-coupled device (CCD) camera, subject chamber, and software. Bioluminescent imaging of the luciferase reporter gene expression will be used to measure the intracellular activity of the clusterin gene. These experiments, which will elucidate the biology of clusterin in vivo for the first time, will enable rapid testing of the bioluminescent imaging device and development of a biodosimeter to monitor radiation exposure in space. Bioluminescent imaging also may have application to bone and cardiovascular diagnostic techniques.

Benefits on Earth

A biodosimeter like the one to be developed during this research could be used to map population radiation exposures following a terrorist attack with a "dirty bomb" radioactive weapon.

Additionally, elucidating the biology of clusterin will contribute to knowledge about carcinogenesis (origins of cancer) caused by radiation and the early effects of radiation exposure. Identification of clusterin production could possibly help to identify persons genetically predisposed for radiosensitivity. Preliminary data show that some people produce high levels of clusterin that may inhibit the suppression of tumors.

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